INTERNATIONAL SEARCH REPORT

[redacted] onal Application No
PCT/IL 99/00524

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N5/06 G01N33/566 G01N33/68 //C07K16/28,C07K14/705

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KONIKOVA E ET AL: "Detection of cytoplasmic and surface membrane markers in cells of some human hematopoietic cell lines." NEOPLASMA, vol. 39, no. 6, 1992, pages 337-42, XP000876522 abstract ---	18,19
A	LÖMS ZIEGLER-HEIBROCK H ET AL: "CD14 is expressed and functional in human B cells" EUROPEAN JOURNAL OF IMMUNOLOGY, vol. 24, no. 8, 1994, pages 1937-40, XP002071627 abstract --- -/--	1-22

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
8 February 2000	21/02/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Le Flao, K

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 96 32418 A (LABORATOIRES OM SA) 17 October 1996 (1996-10-17) page 5, line 17 - line 27 page 7, line 3 - line 15	1-22
A	LIEN E ET AL: "Elevated levels of serum-soluble CD14 in human immunodeficiency virus type 1 (HIV-1) infection: correlation to disease progression and clinical events." BLOOD, vol. 92, no. 6, 15 September 1998 (1998-09-15), pages 2084-92, XP000876524 abstract	1-22

PATENT COOPERATION TREATY

09806689

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
120280.3 MM		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IL99/00524	04/10/1999	04/10/1998
International Patent Classification (IPC) or national classification and IPC C12N5/06		
Applicant TEL-AVIV MEDICAL CENTER RESEARCH & ...et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
27/04/2000	15.01.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Armandola, E Telephone No. +49 89 2399 7493

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/IL99/00524

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:
Description, pages:

1-24 as originally filed

Claims, No.:

1-22 as originally filed

Drawings, sheets:

1/12-12/12 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-22
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-17, 20, 21
	No:	Claims	18, 19, 22
Industrial applicability (IA)	Yes:	Claims	1-22
	No:	Claims	

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: KONIKOVA E ET AL: 'Detection of cytoplasmic and surface membrane markers in cells of some human haematopoietic cell lines.' NEOPLASMA, vol. 39, no. 6, 1992, pages 337-42, XP000876522

D2: LÖMS ZIEGLER-HEIBROCK H ET AL: 'CD14 is expressed and functional in human B cells' EUROPEAN JOURNAL OF IMMUNOLOGY, vol. 24, no. 8, 1994, pages 1937-40, XP002071627

D3: LIEN E ET AL: 'Elevated levels of serum-soluble CD14 in human immunodeficiency virus type 1 (HIV-1) infection: correlation to disease progression and clinical events.' BLOOD, vol. 92, no. 6, 15 September 1998 (1998-09-15), pages 2084-92, XP000876524

D5: TODD R.F. ET AL. : 'Structural analysis of differentiation antigens Mo1 and Mo2 on human monocytes.', HYBRIDOMA, 1982, vol. 1, no. 3, pages 329-337

D4: TODD R.F. AND SCHLOSSMAN S.F.: 'Analysis of antigenic determinants on human monocytes and macrophages.', BLOOD, April 1982, vol. 59, no. 4, pages 775-786

Documents D1 and D2 were not cited in the International Search Report.

Novelty and Inventive step (Art. 33(2)(3) PCT)

i) Claims 1-17, 20 and 21 can be considered novel and inventive for the following reasons: the antigen identified by MAb Mo2, corresponding to CD14, has first been identified on monocytes and macrophages (D1, D2), and later detected also on B-cells (D3) and in soluble form in serum (D4).
Surface expression of CD14/Mo2 on the surface of T cells has not been reported so far. No hint can be found in the available prior art that might have lead the skilled person to the

identification of a population of T lymphocytes which express CD14/Mo2 exclusively intracellularly or to linking the abundance of this cell population to the presence of a bacterial or viral infection in an individual.
The applicant's attention is, however, drawn to the objection made under Item VIII.

ii) Claims 18, 19 and 22, can be considered novel as a kit comprising antibodies binding to the Mo2/CD14 antigen together with antibodies binding to T-cell antigens have not been specifically disclosed in the prior art.
These claims, however, cannot be considered inventive because antibodies to the Mo2/CD14 antigen were known (D1, D2) as well as their use together with antibodies recognizing T-cell antigens in the characterization of lymphocyte populations (D5).
The provision of a kit comprising these antibodies, with or without reference values, cannot be seen as implying the exercise of inventive activity.

Re Item VIII
Certain observations on the international application

Claims 1-7 refer to a population of lymphocytes. In their formulation the claims encompass cells which are part of a human body. The attention of the applicant is drawn to the fact that, should the application enter the regional phase before the EPO, such claims would not fulfill the requirements of Art. 52(2) and Rules 23c(a) and 23e(1) EPC.